

A General Survey of Organic Reactions and Some New Reactions

By

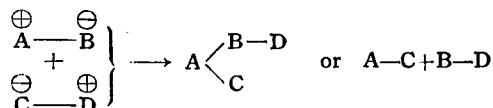
Ryohei ODA

Department of Industrial Chemistry

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I Introduction.

As well known, organic reactions can be divided into two classes; the one is the ionic, and the other is the radical reaction. The ionic reaction can be generally represented as follows:



Here $\text{A} \begin{array}{l} \text{B-D} \\ \text{C} \end{array}$ or A-C represents the aimed reaction product, and B-D represents the by-product such as water in the case of esterification or sodium-halide in the case of ether synthesis. In the case of azo-dyestuffs synthesis, the A-B component, i.e. the diazo-compound, is called the "active component" and the C-D component is called the "passive component". The author has generalized and extended this nomenclature to all organic reactions and has classified the representative organic compounds into active and passive components as shown in the following table:

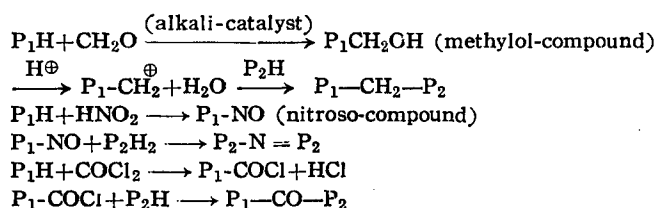
Active Components	Passive Components
1) oxydizing agents	A) reducing agents
2) formaldehyde methylol-compounds	B) ammonia hydrazine hydroxylamine phenylhydrazine semicarbazide, etc.
3) acetaldehyde	
4) benzaldehyde	
5) ethyleneoxide ethylenesulfide epichlorhydrin	C) urea thiourea dicyandiamide melamine, etc.
6) nitrous acid	
7) diazo-compounds	

- 8) carbon monoxide
- 9) carbon dioxide
- 10) carbondisulfide
- 11) nitroso-compounds
- 12) alkyl-halides
chlorformic acid ester
chloracetic acid ester
ethylene chlorhydrin, etc.
- 13) carboxylic acid
acid chlorides
esters
nitriles
acid anhydrides
phosgene, etc.
- 14) diethyl carbonate
orthoformic acid ester
- 15) dimethyl sulfate
sulfonic acid esters
- 16) ketones
pyruvic acid, etc.
- 17) chloroform
carbontetrachloride
- 18) ketenes
carbonsuboxide
- 19) isocyanates
- 20) β -carbon of α , β -unsaturated
carbonyl-compounds
- 21) carbonyl group of active-methylene
compounds
acetoacetic ester
malonic ester
formylacetic ester
formylacetone, e.c.
- 22) sulfenylchloride
- 23) alkylhypochlorite
- 24) amine-halides
- 25) sulfur
sulfurchloride
- 26) halogenes
- 27) sulfuric acid
sulfuric acid anhydride
chlorsulfonic acid
- 28) nitric acid
mixed acid (nitronium-cation)
- D) aniline
naphthylamines
dimethylaniline
aliphatic amines, etc.
- E) phenols
naphthols
- P) ethylene
olefines
rubber
- G) acetylene
phenylacetylene
- H) alcohols
alcoholates
cellulose
- I) mercaptans
isothiurea
thioglycolic acid
thiophenols, etc.
- J) Grignard's reagents
- K) active methyl-compounds
acetaldehyde
acetone
acetic ester, acetonitrile
acetophenone
nitromethane
picoline, etc.
- L) active methylene-compounds
acetoacetic ester
malonic ester
acetylacetone
phenylacetic ester
ketene, etc.
- M) special active methylene-compounds
1,1-di-(p-methoxyphenyl)-ethylene
1,1-di-(p-dimethylaminophenyl)-
ethylene
1,3,3-trimethyl-methylene-indolin
indole, etc.
- N) organo-K-, Na- and Li-compounds
- O) benzene, toluene
- P) naphthalene
anthracene
- Q) halogene-benzenes
- R) bezaldehyde
acetophenone
benzophenone
benzoic acid, etc.
- S) nitrobenzene

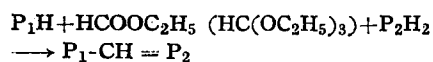
From this table it can easily be understood that all well-known organic reactions or the organic reaction which are practically used for the synthesis of various important technical products take place without exception between the active and the passive components. The author wants to add some notes on the use of this table.

1) In the table there are some compounds which are active components and at the same time are passive components. Acetic ester, acetaldehyde and acetone are some of the examples of this nature. The reason why these compounds occupy the both positions can be understood from the Aldol-condensation or Claisen's ester-condensation, i.e. carbonyl-carbon acts as "active" and the methylgroup as "passive". The author has named this amphotheric character the "two fold behavior of one compound". The same amphotheric character can be seen in active-methylene compounds, ketene and chloroform. Various aromatic derivatives are placed in the table as passive components (O, P, Q, R and S) from the standpoint of nucleus substitution; some of these compounds act naturally also as active components when the substituents have carbonium-cation or nitrogen-cation.

2) Some of the active components are the intermediates of the joint reaction of one active component. For example, the methylol-compounds are the intermediates of the joint reaction by formaldehyde; the nitroso-compounds and diazo-compounds are the intermediates of the joint reaction by nitrous acid; and carbamylchloride and isocyanates are the intermediates of the joint reaction by phosgene. When two passive components are represented as P_1H and P_2H (or P_2H_2) respectively (the passive components generally have the so-called active hydrogen, which tends to separate as proton), the joint reaction can be written in the following manner:



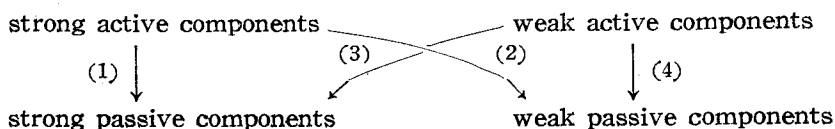
Formic ester and ortho-formic ester also joint two passive components in the following manner:



3) In almost every case of ionic reactions a catalyst is generally used. It is possible to classify catalysts into two kinds. The one is the acidic or Friedel-

Crafts' catalyst and the other is the basic. The author has found that a rule can be established that the acidic catalyst generally strengthens the polarity of the active components while the basic catalyst strengthens on the contrary the polarity of the passive components.

4) Upon surveying the general ionic reactions between the active and passive components from the table, it can generally be said that the reaction depends upon the relative relation between the activity of the active components and the passivity of the passive components. When the activity of the active component is very strong, it reacts with almost every passive component, but when its activity is weak, it can react only with passive components whose passivity is strong enough. Weak active components and weak passive components do not react with one another.



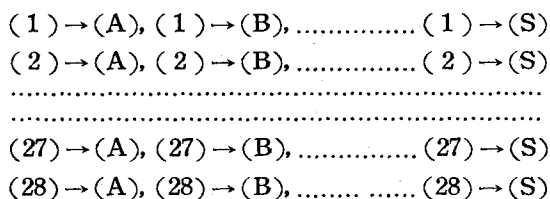
(1): The reaction occurs very easily and vigorously.

(2), (3): The reaction occurs only under a drastic condition.

(4): The reaction does not occur at all.

5) There are some special compounds which react with both the active and the passive components listed in the table. Two examples of these compounds are diazomethane and azides. Though the author has not placed these compounds in the table, their reaction mechanism can be well understood from the viewpoint of the electronic theory.

6) The author wants to emphasize especially that organic chemists should investigate every case of the reactions which can be drawn from the table, as shown below, and see how each reaction occurs.



It must be noted here that there are some compounds of the amphoteric character as already mentioned above (Note 1). Further, as there should be various other compounds, which, though not listed in the table, are very important for organic reactions, it is necessary to take into account these compounds and then extend the table.

7) By doing so, it will be found that not all of the reactions, which can be drawn from the table, have heretofore been exhaustively examined, but that there are some cases which are quite new. For example, the reaction between diazo-compounds (7) and Grignard's reagents (J) has been examined by the author for the first time; the results of examination will be given in the section dealing with the experiment,

It will also be found, that there are many reactions which have been only recently investigated. The author wants to show some of these examples from the literature.

Aldehydes (2), (3), (4) → Ketene (L) (as a passive component)

Hurd, J.A.C.S. 55, 275 (1933)

Kunz, USP. 2, 356, 459

Hagemeyer, Ind. Eng. Chem., 41, 2920 (1949)

Acrylonitrile (27) → Chloroform (as a passive component, not given in the table)

Brunson, J.A.C.S. 67, 601 (1945)

Carbon monoxide (8) → ethylene, olefines (F)

Oxo-synthesis and hydroformylation

Adkins, J.A.C.S. 71, 3051 (1949)

Carbon monoxide (8) → Aniline (D), Hydrazine (B)

Buckley and Ray, J.A.C.S., 71, 1151 (1949)

Esters (13) → Acetylene (G)

Croxall, J.A.C.S., 71, 1261, 1257, 2422 (1949)

Worrall, *ibid.*, 60, 1266 (1938)

Nightingale, *ibid.*, 69, 1181 (1947)

Nitrile (13) → Acetylene (G)

T. L. Cairns, J.A.C.S., 74 3989 (1952)

Diazoniumsalt (7) → Cyclohexanone, Methylketone, Acetone (K)

G. O. Schenk, Z. ang. Chem., 64, 111 (1952)

Amine-halide (22) → double bond (F)

Southwick, J.A.C.S., 74, 1886 (1952)

Sulfenylchloride (20) → Olefin (F), Ketene (L), (M)

R. A. Turner, J.A.C.S., 69, 1009 (1947)

A. Roe, *ibid.*, 70, 1662 (1948) etc.

N. Kharash, *ibid.*, 71, 2724 (1949)

Ketene (18) → 1,3,3-Trimethyl-methylene-indolin (M)

Coenen, Chem. Ber., 80, 546 (1947)

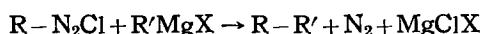
Also in the case of the joint reaction, especially by formaldehyde (Note 2), all of the combinations between R_1H and R_2H have never been exhausted; rather, what portion investigated till now is only about one third or one fourth of the total combinations, and there remains yet a wide domain which must be studied in the future.

In the case of radical reactions, it has not yet been possible to establish

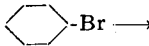
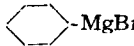
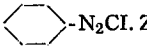
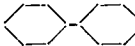



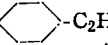
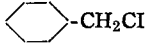
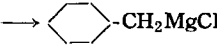
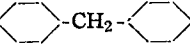
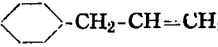
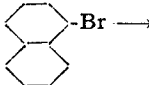
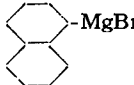

such a general systematic survey as in the case of ionic reactions, but the radical reaction has become recently a great object of researches. The author has made also some interesting investigations on radical reactions and wants to report them in the section treating of the experiment together with the ionic reactions.

II. Experiment.

1) The reaction between diazo-compounds and Grignard's reagents, a new reaction (7) → (J)

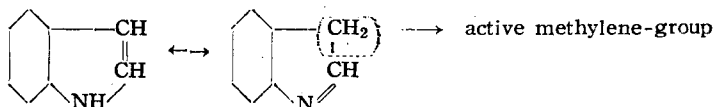


Experimental procedure: As Grignard's reaction occurs only in absolute ether, diazoniumsalt was first converted into $ZnCl_2$ -double salt and perfectly dried. To a cooled suspension of this double salt in ether Grignard's solution was added slowly while stirring. A more or less vigorous reaction occurs under the evolution of nitrogen, After 24 hrs a mixture of ice water and HCl was added and the insoluble resinous product was filtered out. The filtered ether solution was dried with $CaCl_2$; ether evaporated and the residue was purified appropriately. The results obtained are summarized in the following table:

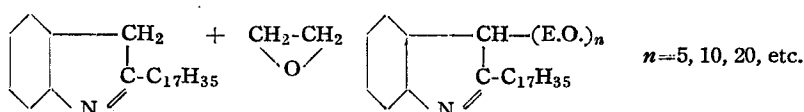
		Product	(yield)
 -Br → 	 -N ₂ Cl · ZnCl ₂		(8 g)
33 g (0.2 mole)	40 g (0.19 mole)		
Br-  -Br → Br- 	"	Br- 	(10 g)
47 g (0.2 mole)	30 g (0.14 mole)		
C ₂ H ₅ Br → C ₂ H ₅ MgBr	"		(4 g)
33 g (0.3 mole)	30 g (0.14 mole)		
 -CH ₂ Cl → 	"		(7 g)
35 g (0.28 mole)	55 g (0.26 mole)		
CH ₂ =CH-CH ₂ -Br → CH ₂ =CH-CH ₂ -MgBr	"		(20 g)
25 g (0.21 mole)	40 g (0.19 mole)		
 -Br → 	"		(2 g)
25 g (0.12 mole)	35 g (0.16 mole)		

2) The reaction between ethyleneoxide and 2-heptadecyl-indole, a new reaction (5) → (M)

Indole can be considered as one kind of an active methylene-compound.

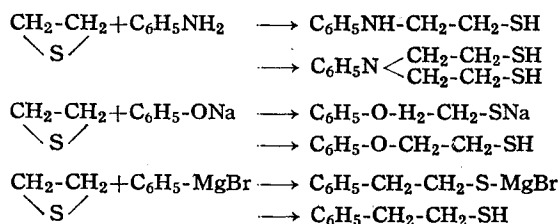


Indeed on the 3-position of indole or indolenine act various active components, but till now no publication has appeared in which ethyleneoxide is taken into account. The author has selected 2-heptadecylindole instead of indole itself, in order to obtain a new kind of non-ionic surfactant. Using KOH as a catalyzer (ca. 3~5 weight % to indole), gaseous ethyleneoxide was passed through molten 2-hepadecyl-indole and thus the aimed 3-polyoxyethyl-2-heptadecyl-indole was obtained, and it is found that this new compound has an excellent character as non-ionic surfactant.



3) The reaction between ethylenesulfide and aniline, phenol and Grignard's reagent, a new reaction (5) → (D), (E), (J).

It can easily be anticipated that ethylenesulfide will react as an active component quite analogously to ethyleneoxide on various passive components. But the chemical nature of ethylenesulfide was only recently investigated to some degree precisely. The author has undertaken to examine the reaction between ethylenesulfide and aniline, phenolate and Grignard's reagent, and ascertained the following:



4) Decomposition of diazoniumsalt-zincchloride double salt in inert solvents.

As an indirect method for introducing the halogen in the aromatic nucleus so-called Sandmeyer's or Gattermann's process is usually employed. The author has found a new method for the same purpose. This method consists of refluxing diazoniumsalt-zincchloride double salts in a proper inert solvent such as ether, benzene or toluene. Some double salts decompose easily in halogen benzene at the boiling point of ether, but others not so easily.

In the latter case it is advisable to use other solvents which boil at higher points than ether. When the decomposition in benzene is not sufficient, toluene must be used.

These results are given below :

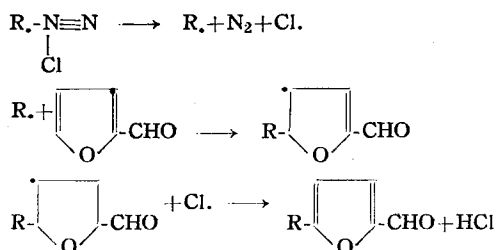
Aniline	$\xrightarrow{\text{ether}}$	Chlorbenzene	yield 79%
m-Toluidine	$\xrightarrow{\text{ether}}$	m-Chlortoluene	85%
o-Toluidine	$\xrightarrow{\text{ether}}$	o-Chlortoluene	84%
p-Toluidine	$\xrightarrow{\text{benzene}}$	p-Chlortoluene	75%
m-Xylidine	$\xrightarrow{\text{ether}}$	Chlor-m-xylene	80%
m-Chloraniline	$\xrightarrow{\text{benzene}}$	m-Dichlorbenzene	70%
p-Chloraniline	$\xrightarrow{\text{benzene}}$	p-Dichlorbenzene	36%
"	$\xrightarrow{\text{toluene}}$	"	68%
p-Nitraniline	$\xrightarrow{\text{benzene}}$	p-Nitrochlorbenzene	35%
"	$\xrightarrow{\text{toluene}}$	"	73%
m-Nitraniline	$\xrightarrow{\text{toluene}}$	m-Nitrochlorbenzene	67%
o-Nitraniline	$\xrightarrow{\text{toluene}}$	o-Nitrochlorbenzene	30%
p-Anisidine	$\xrightarrow{\text{toluene}}$	p-Chloranisol	26%
o-Anisidine	$\xrightarrow{\text{toluene}}$	o-Chloranisol	25%
β -Naphthylamine	$\xrightarrow{\text{benzene}}$	β -Chlornaphthalene	78%
Tolidine	$\xrightarrow{\text{benzene}}$	p-p'-Dichlor-m-m'-di- mehtyl-diphenyl	70%
α -Naphthylamine	$\xrightarrow{\text{benzene}}$	α -Chlornaphthalene	77%
Benzidine	$\xrightarrow{\text{benzene}}$	p-p'-Dichlordiphenyl	65%

5) Radical Reaction.

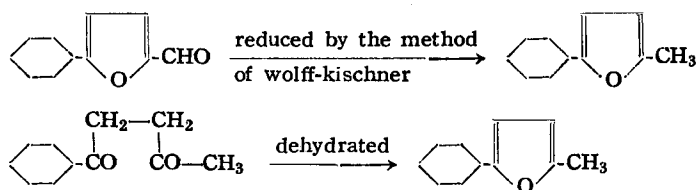
Meerwein's reaction between diazoniumsalt and furfural, furancarboxylic acid, furfurylidene acetone and furylacrylic acid.

The author has found that Meerwein's reaction occurs between various aromatic diazoniumsalts and furfural, furancarboxylic acid, furfurylidene acetone, furylacrylic acid and furan.

Meerwein's reaction is understood nowadays as a radical reaction and therefore the reaction shema can be written as follows:

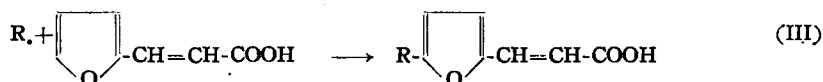
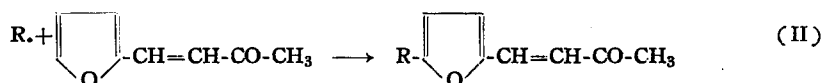


The position of the attack of R. radical was decided as the 5-position of furfural in the following manner:

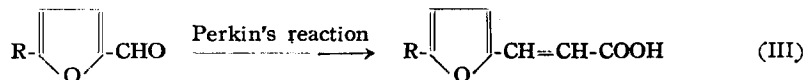
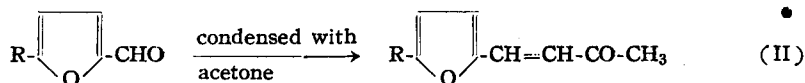
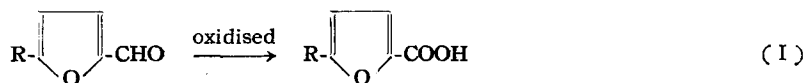


The both methyl-phenyl-furans, produced on the one hand by the reduction of the reaction product, and on the other from phenacylacetone by dehydration, were quite identical.

The reactions between diazoniumsalts and furancarboxylic acid, furfurylideneacetone, furylacrylic acid occur also at the 5-position of furan-ring.



(I), (II) and (III) were prepared otherwise respectively from the arylfurfural, obtained in the manner mentioned above, and the identity in each case was proved.



From these results it can be concluded that Meerwein's reaction does not occur at the double bond of the side chain of furfurylideneacetone and furylacrylic acid, though this is the case by cinnamic acid.

Some experimental data are given in the following table:

Diazoniumsalt	product	yield	m. pt.
<chem>Clc1ccc(N=[N+]Cl)cc1</chem>	5-(p-chlorophenyl)-furfural	66% in acetone 90% in water	128-129°
<chem>[O-][N+]([O-])c1ccc(N=[N+]Cl)cc1</chem>	5-(p-nitrophenyl)-furfural	89% in acetone 96% in water	203-204°
<chem>c1ccc(N=[N+]Cl)cc1</chem>	5-phenylfurfural	47% in acetone 49% in water	(oil)
<chem>O=S(=O)c1ccc(N=[N+]Cl)cc1</chem>	5-(p-sulfophenyl)-furfural	44% in acetone 39% in water	—
<hr/>			
<chem>Clc1ccc(N=[N+]Cl)cc1</chem>	5-(p-chlorophenyl)-furfurylidene-acetone	30%	(b. pt. 150-158°/40 mm)
<hr/>			
<chem>Clc1ccc(N=[N+]Cl)cc1</chem>	5-(p-chlorophenyl)-furylacrylic acid	26%	223-225°
<chem>[O-][N+]([O-])c1ccc(N=[N+]Cl)cc1</chem>	5-(p-nitrophenyl)-furylacrylic acid	30%	203-204°
<hr/>			
<chem>c1ccc(N=[N+]Cl)cc1</chem>	5-phenyl-furan-carboxylic acid	60%	(b. pt. 120-122°/30 mm)
<chem>Clc1ccc(N=[N+]Cl)cc1</chem>	5-(chlorophenyl)-furan-carboxylic acid	93%	197-198°
<chem>[O-][N+]([O-])c1ccc(N=[N+]Cl)cc1</chem>	5-(p-nitrophenyl)-furan-carboxylic acid	96%	230-231°

An example of the experimental procedure :

9 g p-nitroaniline was diazotized as usual and to this diazo-solution was added a solution of 8 g furfural in 50 cc acetone (or water), and then 3 g cupric chloride, dissolved in water, was added drop by drop wise while stirring at 20-30° and further stirred for 3-4 hrs. After the removal of volatile matter by steam distillation, the residue was collected and recrystallized from acetone, yellow crystals, m. pt. 203-204°, yield 16 g.

	C: 61.36%	H 3.81%
calculated ;	(60.83%)	(3.26%)

N-content of semicarbazone of p-chlorophenyl-furfural was 15.80% (calculated 15.93%).

As well known, furfural can be easily converted into black resin by treating with mineral acids.

Obtained arylfurfural can also be converted into a black body by the same treatment. The author has found that a new bluish black acid dye can be obtained from p-sulfophenyl-furfural, in this dye chromophor being the converted furaning, although its structure is not clearly known.

As proved above experimentally, furfural is an interesting radical acceptor in the radical reaction.

The author has also found that the radical, produced easily from azo-

isobutyric acid nitrile, can also attack furfural, and that 5-(α -nitrilo-isopropyl)-4,5-dihydro-furfural is obtained, as shown in the following schema:

